ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA
DIPARTIMENTO DI SCIENZE MEDICHE VETERINARIE

Dottorato di ricerca in Scienze Veterinarie
[XXXV] CICLO - A.A. [2021/2022]
CURRICULUM: Scienze di Base
Anno di attività: [3°/3°]
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Development of a porcine lactation model for the evaluation of mammary clearance of exogenous molecules

Introduction

Nowadays, the importance of breastfeeding has been well recognized by the scientific world and public opinion [1]. Such awareness has nonetheless put a lot of pressure on women under chronic pharmacological medication, or that simply undergo common post-partum health issues, due to the lack of scientific data regarding the potential transfer to the offspring [2]. In such scenario, Task 3.3 of the ConcePTION project is aimed to develop and characterize an *in vivo* animal model for drug passage from maternal blood to breast milk; the swine species was chosen upon accurate literature review.

Part 1:

animals — MDPI

Review

Animal Models for In Vivo Lactation Studies: Anatomy, Physiology and Milk Compositions in the Most Used Non-Clinical Species: A Contribution from the ConcePTION Project

Domenico Ventrella [1], Nurit Ashkenazi [2], Alberto Elmi [1,*], Karel Allegaert [3,4,5], Camilla Aniballi [1], Anthony DeLise [6], Patrick John Devine [7], Anne Smits [3,8], Lilach Steiner [2], Monica Forni [1], Michele Bouisset-Leonard [9] and Maria Laura Bacci [1]

About ConcePTION

Acknowledgements: This work has received support from the EU/EFPIA Innovative Medicines Initiative [2] Joint Undertaking ConcePTION grant n° 821520.

Part 2:

Building an animal lactation model: pilot amoxicillin study in conventional pigs and Göttingen minipigs

A contribution from the ConcePTION project

Aniballi C.(1), Ventrella D. (1), Elmi A. (1), Johanne Hansen M.(2), Rosenmay Jacobsen K. (2), Van Daele J.(3), Armoudjian Y. (3), Bertocchi M. (1), Ashkenazi N.(4), Anderson B.(5), Delise A.(6), Bouisset-Leonard M. (6), Forni M. (1), Bacci M.L. (1)
(1) University of Bologna; (2) Ellegaard Göttingen Minipigs; (3) BioNotus GCV; (4) Teva Pharmaceutical Industries; (5) Covance Laboratories; (6) Novartis Pharma AG

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Materials and Methods

6 pregnant sows:

3 conventional hybrids

3 Göttingen Minipigs

Amoxicillin 7 mg/kg IM SID to lactating sows

Daily training

Lactation week 2 | Lactation week 3 | Lactation week 4

d-30 … d0 d1 d2 d3 d4 d5 d6 d7 d8 d9 d10 d11 d12 d13 d14 d15 d16 d17 d18 d19 d20 d21 d22 d23 d24 d25 d26 d27 d28

Parturition

Peripheral vascular long-term catheter for sows blood samplings

PK on first dosing day:
11 maternal blood samples within 24h

SOW DAYS: 4 matched maternal milk/blood samples per day

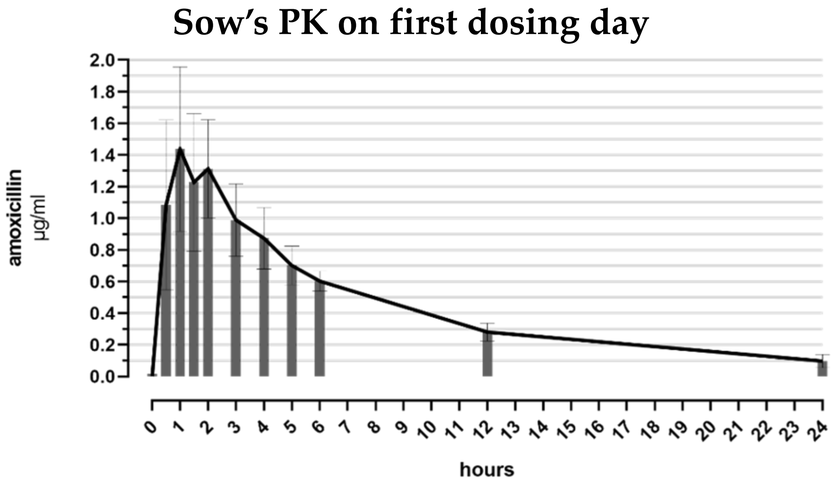
- ✓ Pre-amoxi
- ✓ 2h post-amoxi
- ✓ 4h post-amoxi
- ✓ 8h post-amoxi

SOW + PIGLETS DAYS: 2 matched maternal/piglets timepoints per day

- ✓ Sow blood/milk pre-amoxi
- ❖ Piglets plasma pre-amoxi
- ✓ Sow blood/milk 2h post-amoxi
- ❖ Piglets plasma 2.5h post-amoxi

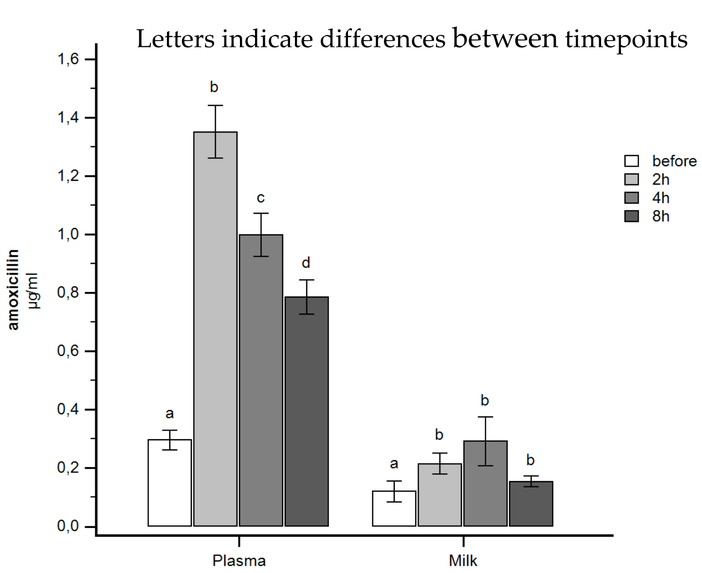
Results

Sow's PK on first dosing day



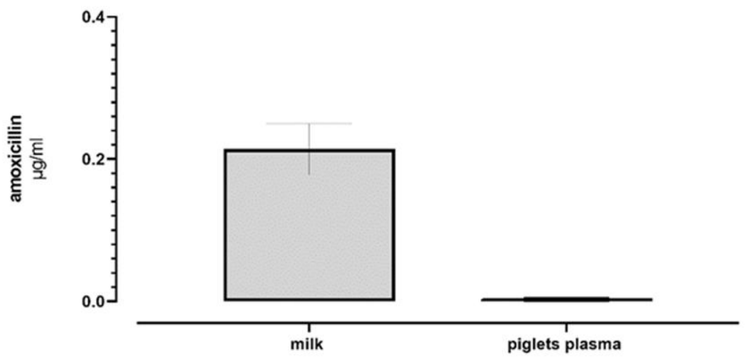
- Highest plasma concentrations 2h post-amoxi
- Highest milk concentrations 4h post-amoxi

Sows' plasma/milk amoxicillin concentrations



Amoxicillin in sows' milk and piglets' plasma

- Amoxicillin was not quantifiable in piglets' plasma 2.5h after maternal administration



Conclusions

Overall, the study design used for this preliminary trial has allowed to highlight both strengths and critical points of this new model to test infant drug exposure through milk. As for the quantification of amoxicillin in the different matrices, the results seem to be consistent between sows. The procedures were feasible and well tolerated by animals; this is extremely important when assessing the ethical impact of the trials.

References

[1] Lawrence, R. M., & Lawrence, R. A. (2022). Breastfeeding in a New Era. In Breastfeeding (pp. 1-37). Elsevier.

[2] Ventrella, D., Forni, M., Bacci, M. L., & Annaert, P. (2019). Non-clinical models to determine drug passage into human breast milk. Current Pharmaceutical Design, 25(5), 534-548.